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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/423,698	02/10/2000	ODILE LEROY	99849-A	7060

7590

07/21/2003

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EXAMINER

DUFFY, PATRICIA ANN

ART UNIT

PAPER NUMBER

1645

DATE MAILED: 07/21/2003

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Please find below and/or attached an Office communication concerning this application or proceeding.

## Office Action Summary

Application No.  
**09/423,689**Applicant(s)  
**Leroy**Examiner  
**Patricia A. Duffy**Art Unit  
**1645**

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE three MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on Jul 15, 2002
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1-24 is/are pending in the application.
- 4a) Of the above, claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☐ Claim(s) \_\_\_\_\_ is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☒ Claims 1-24 are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on \_\_\_\_\_ is: a) ☐ approved b) ☐ disapproved by the Examiner.  
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

### Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).  
a) ☐ All b) ☐ Some\* c) ☐ None of:  
1. ☐ Certified copies of the priority documents have been received.  
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_  
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).  
\*See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).  
a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

### Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892) 4) ☐ Interview Summary (PTO-413) Paper No(s). \_\_\_\_\_
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). \_\_\_\_\_ 6) ☐ Other:

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#### DETAILED ACTION

1. The finality of the rejection of the last Office action is withdrawn in view of the new rejections set forth below.
2. All rejections are withdrawn in view of the new rejections set forth below.
3. The Examiner of U.S. Patent application SN 09/423,698 has changed. In order to expedite the correlation of papers with the application please direct all future correspondence to Examiner Patricia A. Duffy, Group 1600, Art Unit 1645.

#### *Priority*

4. Receipt is acknowledged of papers submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file. Additionally, receipt is acknowledged of the certified translation of the French priority document.

#### *Claim Rejections - 35 U.S.C. § 112*

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:  
  
The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

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6. Claims 1-24 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

As to claims 1 and 16 and every claim dependent thereon remain indefinite from the use of the term "derived from" as set forth in the previous office actions of record. Applicants argue specific process limitations from the specification that are not in the claims.

As to claim 6 and every claim dependent thereon, the acronyms A1 and A2 are prima facie indefinite because the specification does not define the metes and bounds of these protein carriers.

As to claim 7, it is impossible to ascertain what this claim is directed to. What is "A1" and what is "A2" and what do these represent? What is the function of " $n/2$ "? This appears to be a mathematical expression or ratio? Further, claim 1 requires that at least one  $P_n$  be different, however claim 7 appears to assign the identical  $P_n$  both A1 and A1. Claim 7 recites when " $n$ " is an even number, " $n/2$  proteins  $P_1$  to  $P_n$  are A1 and " $n/2$  carrier proteins  $P_1$  to  $P_n$  are A2". How can the carrier be both A1 and A2 at the same time? The same issue arises with the odd notations. As such, it is unclear how the claim is assigning either A1 or A1 as the carrier protein. Is Applicant intending to assign the even numbered " $P_n$ " to A1 (what ever that is) and the odd numbered " $P_n$ " to A2? The language is so

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confusing that it does not appear to further limit the claims from which it depends because claim 1 requires that at least one carrier protein be different from the others.

Clarification and correction are respectfully requested.

As to claims 10 and 16 and every claim dependent thereon, the claim is unclear because "Dt" alone is not part of the composition and the term dose lacks antecedent basis in the claim from which it depends.

As to claims 11 and 16 and every claim dependent thereon, the claim is unclear because "Tt" alone is not part of the composition and the term dose lacks antecedent basis in the claim from which it depends.

As to claim 12, and every claim dependent thereon, the claim is confusing because it comprises 10 or 11 valences represented by 10 or 11 conjugates and the term valences appears equivalent to conjugates and is thus duplicative in nature. What is the intended difference between valences and conjugate. Additionally, the term valences does not have antecedent basis in the claim.

As to claim 14, the claim is unclear because it does not use the terminology of claim 1 such as Pn for polysaccharides and Cn for conjugates as such it is not clear in its antecedent basis as it dependent from claim 1.

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*Claim Rejections - 35 U.S.C. § 102*

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103© and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

8. Claims 1-24 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chu et al (Infection and Immunity, 40(1):245-256, April 1983) in view of Merck and Co. Inc. (EP 0497 525, May 8, 1992).

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Chu et al teach a composition comprising two or more conjugates comprising a bacterial polysaccharide coupled to a carrier protein. In particular, when two or more conjugates were injected they were admixed in a single syringe (see page 247, column 2, "Immunization"). Chu et al teach the combination of Haemophilus influenzae Type b (Hib) and Pneumococcal Type 6A polysaccharide (Pn6A) protein conjugates. Hib was conjugated to horseshoe crab hemocyanin (HCH) and Pn6A was conjugated to tetanus toxin (TT) and were administered together. Additionally, the polysaccharide K100 from E. coli was conjugated to TT or to HCH and was administered in combination with either Hib-HCH or Hib-TT respectively (see page 249, Table 2). The Hib and K100 conjugates were administered at 1.25 ug of polysaccharide and when in combination with Pn6A, each was injected at 2.5 ug polysaccharide. At these levels, the levels of TT or HCH administered is below 50 ug/dose (see Table 1). Chu et al also teach that when Hib-HCH was injected with either Pn6A-HCH or Pn-TT, both the anti-Hib and anti-Pn6A responses were increased over that induced by either conjugate alone. Chu et al also teach that the injection of two conjugates did not exert a negative effect (page 253, column 1, first full paragraph). Chu et al teach that the experiments have shown that a "useful" carrier is as effective as a "nonsense" carrier in mice. Therefore, it would seem that a "useful" carrier would be preferred in human use (page 254, column 1, first full paragraph). Chu et al differ by not teaching conjugation of the Hib polysaccharide with diphtheria toxin (Dt).

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Merck and Co. Inc. teach conjugates of partially hydrolyzed, highly purified, capsular polysaccharide (Ps) from *Streptococcus pneumoniae* serotypes 1, 2, 3, 4, 5, 6B, 7F, 8, 9N, 9V, 10A, 11 a, 12F, 14, 15B, 17F, 18C, 19F, 19A, 20, 22F, 23F and 33F conjugated to a protein moiety (PRO) wherein the PRO that should behave as an immune enhancer and that such immune enhancers are the outer membrane protein complex (OMPC) derived from *Neisseria meningitidis*, tetanus toxin, diphtheria toxin or pertussinogen may be used. Merck and Co. Inc, teach vaccines comprising a mixture from one to ten different pneumococcal polysaccharide-immunogenic protein conjugates (Pn-Ps-PRO) induce broadly protective recipient immune responses against cognate pathogens (see abstract). Merck and Co. Inc. indicate that polyvalent vaccines comprising 23 unconjugated *Streptococcus pneumoniae* (Pn) polysaccharides is commercially available as "PNEUMOVAX™23" and accounts for 90 percent of pneumococcal blood isolates. Merck and Co. Inc, teach that the unconjugated vaccines are least effective in the elderly and infants under 2 years, and this is the segment of the population most at risk for pneumococcal infections. Merck and Co. Inc. teach that since unconjugated polysaccharides are poor inducers of T-cell immune responses, conversion of the Pn-Ps into immunogens capable of inducing T-cell responses is the key to producing adequate protection in this target population. (see page 2, second full paragraph).

As to claims 1-12 and 14 it would have been *prima facie* obvious to one of ordinary skill in the art to modify the conjugate composition of Chu et al by combining any of the

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additional Pn-Ps-PRO conjugates of Merck and Co Inc. to provide for a conjugate vaccine containing up to 10 different Pn-Ps-PRO conjugates because Merck and Co Inc. teach that vaccines comprising a mixture from one to ten different pneumococcal polysaccharide-immunogenic protein conjugates (Pn-Ps-PRO) induce broadly protective recipient immune responses against cognate pathogens and Merck and Co Inc teach that the PRO portion of the conjugate may be an immune enhancer such as TT or DT. As to claims 16, 17, 18 and 21, it would have been *prima facie* obvious to one having ordinary skill in the art at the time that the invention was made to substitute the protein Dt of Merck and Co Inc for the HCH in the Hib-HCH conjugate of Chu et al because Chu et al teach that a "useful" carrier would be preferred in human use (page 254, column 1, first full paragraph) and Merck and Co. Inc. teach that PRO that should behave as an immune enhancer and that such immune enhancers are the outer membrane protein complexes (OMPC) derived from *Neisseria meningitidis*, tetanus toxin, diphtheria toxin or pertussinogen may be used in conjugate vaccines for human use. As to claims 1<sup>to</sup>24, it would have been further *prima facie* obvious to one of ordinary skill in the art to modify the conjugate composition of Chu et al by adding any of the additional Pn-Ps-PRO conjugates of Merck and Co Inc. to provide for a conjugate vaccine containing up to 23 different Pn-Ps-PRO conjugates because Merck and Co Inc. teach that vaccines comprising a mixture of different pneumococcal polysaccharide-immunogenic protein conjugates (Pn-Ps-PRO) induce broadly protective recipient immune responses against

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cognate pathogens, Merck and Co Inc teach that the PRO portion of the conjugate may be an immune enhancer such as TT or DT and the combination of all 23 polysaccharide serotypes would provide the benefit of covering 90 percent of pneumococcal blood isolates (disease causing).

*Status of Claims*

9. No claims are allowed. All claims stand rejected.
10. Any inquiry of a general nature or relating to the status of this general application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Papers relating to this application may be submitted to Technology Center 1600, Group 1640 by facsimile transmission. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). Should applicant wish to FAX a response, the current FAX number for Group 1600 is (703) 308-4242.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Patricia A. Duffy, Ph.D. whose telephone number is (703) 305-7555. The examiner can normally be reached on Monday-Friday from 9:30 AM to 6:00 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith, can be reached at (703) 308-3909.

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Patricia A. Duffy, Ph.D.

July 18, 2003

*Pat A Duffy*

Patricia A. Duffy, Ph.D.

Primary Examiner

Group 1600